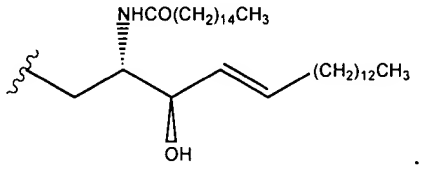
antibody might also have the capacity to recognize higher order fucosylated arrays.

REMARKS

Claims 108-119 are currently pending in the application. Claims 112 and 113 are allowed. Claims 109, 111, 114, 115 and 117-119 are rejected under 35 U.S.C. § 112, second paragraph. Claims 108, 110, 114 and 116 are rejected under 35 U.S.C. § 102(b). Claims 109 and 115 have been canceled and claims 108, 110-111, 114 and 116-118 have been amended. Claims 112-113 and 119 remain unchanged. Applicant respectfully requests entrance of the amendments as detailed above for the above-referenced patent application and submits that the amendments do not present new matter. The present amendments are not in acquiescence to any position taken by the Examiner, but are made solely to expedite prosecution of the subject matter now claimed, and are thus made without disclaimer or prejudice to prosecution of claims to any subject matter which may have been lost at this time by virtue of the amendments. Applicant additionally reserves the right to re-introduce the subject matter of any of the canceled claims in continuing or divisional applications.

Amendments to Claims

Claim 108 has been amended to incorporate the subject matter of claim 109. Amended claim 108 also includes the proviso that "when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1)", support for which can be found *inter alia* in original claim 108. Claim 110, as amended, finds support *inter alia* in original claim 110. Group R, as defined in newly amended claim 110, does not include substituted or unsubstituted alkyl or aryl, or a moiety having the structure:



Claims 111, 117 and 188 have been amended to correct claim dependency. Claim 116, as amended, finds support *inter alia* in original claim 116. Claim 114 has been amended to place it in independent form, and to remove the word "optionally", as suggested by the Examiner.

Applicant respectfully submits that no new matter is introduced with these amendments.

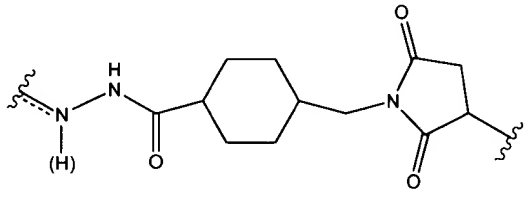
Amendments to the specification

As required by the Examiner, the specification has been amended to recite the correct page number for the Nature Structural Biology publication. With respect to amendment to the paragraph found at page 1 lines 6-12 of the specification introduced in the Preliminary Amendment filed with this application on April 12, 2002, Applicant has canceled that Amendment, and has entered a new Amendment deleting and replacing it with a newly amended paragraph. Applicant respectfully submits that no new matter is introduced with these amendments.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 109, 111, 114, 115 and 117-119 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Specifically, the Examiner states that recitation of "a composition comprising the compound of claim 108" (*e.g.*, in claim 114) does not impart patentable distinctness to the product of claim 108. Applicant has amended claim 114 to remove the word "optionally", thereby obviating the rejection.

In addition, the Examiner has rejected claims 109 and 115 for reciting an "M_2 linker" without defining it as such. Claims 109 and 115 have been canceled, thereby rendering the rejection moot. Applicant notes that newly amended claims 108, 110 and 116 recite an "M_2 linker having the structure:  ", and submits that these claims are perfectly clear to the practitioner skilled in the relevant art.

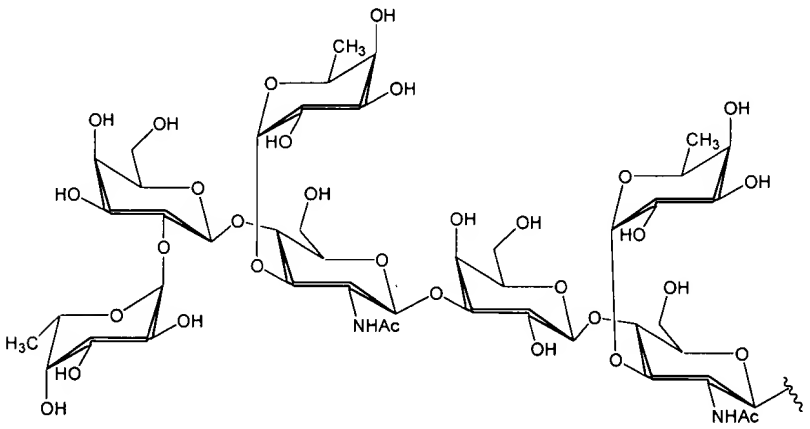
In view of the remarks above, Applicant respectfully requests that the stated rejections be withdrawn.

Rejections under 35 U.S.C. § 102(b)

Claims 109 and 115 have been canceled, and claims 108, 110-111, 114 and 116-118 have been amended, however, in an effort to expedite prosecution, the stated rejections will be addressed as if they were applied to the claims, as newly amended.

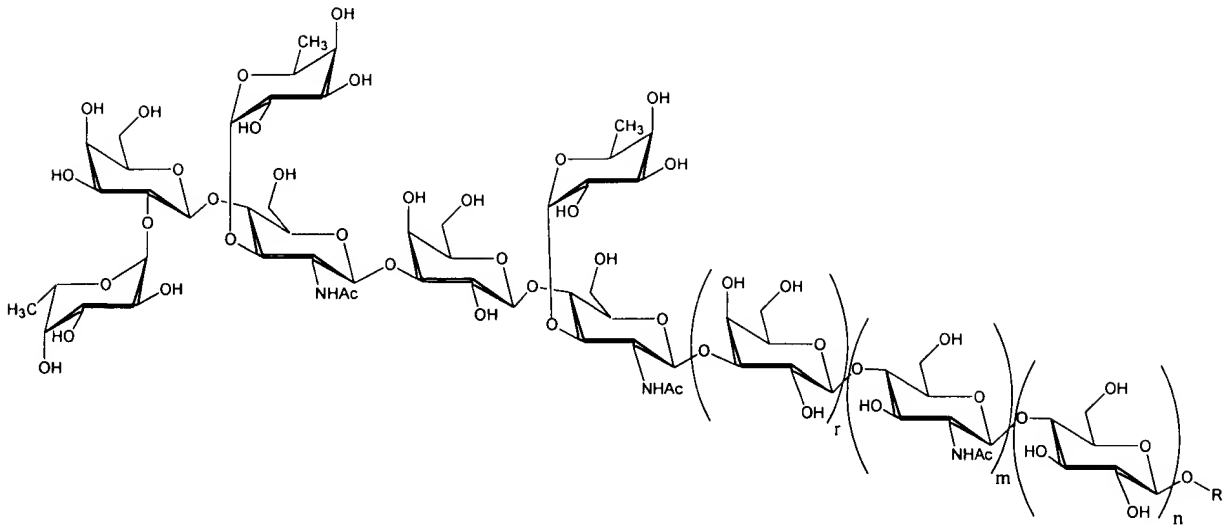
A. The Examiner has rejected claims 108, 110, 114 and 116 under 35 U.S.C. § 102(b) as being anticipated by any one of Windmüller *et al.* (Tetrahedron Letters, 1994, Vol. 35, pp. 7927-7930) or Helland *et al.* (Journal of Carbohydrate Chemistry, 1992, Vol. 11, pp. 77-80). The Examiner states that Windmüller *et al.* disclose the chemical synthesis of the determinant of claim 110 (citing structure 2c on page 7929), where the set of indices (r, m, n) is (1, 0, 1) and wherein R is a substituted alkyl group. The Examiner also alleges that Helland *et al.* disclose the chemical synthesis of the determinant of claim 110 (citing structure 13 on page 80), where the set of indices (r, m, n) is (1, 0, 1) and wherein R is a substituted alkyl group. With respect to structure 13 on page 80 of the Helland *et al.* reference, Applicant notes that it only comprises 7 saccharide units. Therefore, Applicant assumes that the Examiner meant to compare Helland's structure 13 with the determinant of claim 110 where the set of indices (r, m, n) is (0, 0, 0), not (1, 0, 1). In an effort to expedite prosecution, Applicant will address the rejection accordingly.

Claim 108, as amended, is directed to a compound having the determinant:



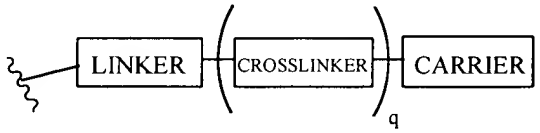
wherein the compound is bound to a suitable carrier protein or lipid. Helland does not teach carbohydrate constructs attached to a carrier protein or lipid. Therefore Helland does not anticipate newly amended claim 108. Likewise, with the exception of compound 2c on page 7927 of the Windmüller *et al.* reference, Windmüller does not teach compounds having the determinant of claim 108, wherein the compound is bound to a suitable carrier protein or lipid. With respect to Windmüller's compound 2c, Applicant notes that claim 108 includes the proviso that "when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1)", and thus claim 108, as amended, specifically excludes Windmüller's compound 2c. Therefore Windmüller does not anticipate newly amended claim 108.

Claim 110, as amended, is directed to a compound having the structure:



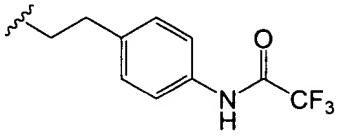
wherein r, m, and n are independently 0, 1, 2 or 3;

R is H, substituted or unsubstituted allyl, an amino acyl moiety, or a moiety having the structure:



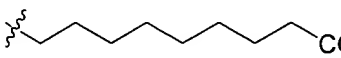
wherein q, the linker, crosslinker and carrier are as defined in claim 110.

The compounds disclosed in the Helland *et al.* reference do not fall within the scope of claim 110, as amended. Specifically, with respect to structure 13 on page 80 of the Helland *et al.* reference, the moiety having the structure:



does not fall within the definition of R as set out in newly amended claim 110. Therefore Helland does not anticipate newly amended claim 110.

Likewise, the compounds disclosed in the Windmüller *et al.* reference do not fall within the scope of claim 110, as amended. Specifically, with respect to structure 2c on page 7927 of the Windmüller *et al.* reference, the moiety having the structure:



does not fall within the definition of R as set out in newly amended claim 110. Therefore Windmüller does not anticipate newly amended claim 110.

Claims 114 and 116, as amended, are directed to compositions comprising a compound of claim 108 and 110, respectively, and an immunological adjuvant and/or a pharmaceutically acceptable carrier. Neither Helland nor Windmüller teach compositions comprising an immunological adjuvant and/or a pharmaceutically acceptable carrier. Therefore, the Helland and Windmüller references cannot anticipate claims 114 and 116.

In view of the remarks above, Applicant respectfully submits that the Windmüller *et al.* and/or the Helland *et al.* reference(s) do not anticipate the instant claims. Accordingly, Applicant respectfully requests that the stated rejection be withdrawn.

B. The Examiner has rejected claims 108, 110 and 114-116 under 35 U.S.C. § 102(b) as being anticipated by Nudelman *et al.* (The Journal of Biological Chemistry, 1986, Vol. 261, pp. 11247-11253). The Examiner states that Nudelman *et al.* disclose the isolation and structural determination of compounds having the determinant of claims 108 and/or 110, wherein the set of indices (r, m, n) is (1, 0, 1), the determinant is bound to a –linker-(crosslinker)$_q$-carrier moiety, wherein the linker is –$(CH_2)_s$- wherein s is 2, q is 0, and the carrier is a lipid (citing the phytosphingosines referred to in figure 4B on page 11251 of the Nudelman *et al.* reference).

Applicant notes that claim 108 includes the proviso that "when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1)", and thus excludes the compounds disclosed in the Nudelman *et al.* reference. One of ordinary skill in the art will appreciate that phytosphingosines are ceramides (see, for example, the paragraph bridging columns 1 and 2 on page 11250 of the Nudelman *et al.* reference, which reads: "*Ceramide composition is indicated by the ions shown in Fig. 4B. In particular, the A series (31) appears characteristic of ceramides containing phytosphingosine, which is also represented by the ion at m/z 396. [...] Previously, these have been seen in the electron impact mass spectra of H type 1 chain fucolipid isolated from human plasma (31), Le^b fucolipid from dog intestine (32), and fucolipids isolated from human meconium (10), attributable in each case to ceramides containing phytosphingosine and saturated α-hydroxy fatty acids.*" Accordingly, Nudelman cannot anticipate claim 108.

Likewise, claim 110 also includes the proviso that "when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1)", and thus specifically excludes the compounds disclosed in the Nudelman *et al.* reference. Therefore, Nudelman cannot anticipate claim 110.

Claims 114 and 116, as amended, are directed to compositions comprising a compound of claim 108 and 110, respectively, and an immunological adjuvant and/or a pharmaceutically acceptable carrier. Nudelman does not teach compositions comprising an immunological adjuvant and/or a pharmaceutically acceptable carrier. Therefore, the Nudelman reference cannot anticipate claims 114 and 116.

In view of the remarks above, Applicant respectfully submits that the Nudelman *et al.* reference(s) does not anticipate the instant claims. Accordingly, Applicant respectfully requests that the stated rejection be withdrawn.

C. The Examiner has rejected claims 108, 110, 114-116, 118 and 119 under 35 U.S.C. § 102(b) as being anticipated by Kaizu *et al.* (The Journal of Biological Chemistry, 1986, Vol. 261, pp. 11254-11258). The Examiner states that Kaizu *et al.* teach a composition of Le^y trifucosylceramide and salmonella Minnesota cells (citing the paragraph entitled "Materials and Methods on page 11254 of the Kaizu *et al.* reference).

Applicant notes that claims 108, 110, 114 and 116 include the proviso that "when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1)", and thus, claims 108, 110, 114 and 116 specifically exclude the Le^y trifucosylceramide. Therefore, Kaizu cannot anticipate claims 108, 110, 114 and 116, as amended, and claims dependent thereon (*e.g.*, claims 118 and 119).

In view of the remarks above, Applicant respectfully submits that the Kaizu *et al.* reference(s) does not anticipate the instant claims. Accordingly, Applicant respectfully requests that the stated rejection be withdrawn.

Double Patenting Rejection

The Examiner has provisionally rejected claims 108, 110, 114 and 116 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5 and 10 of co-pending Application No.: 09/794,905. The Examiner states that claims 5 and 10 of the '905 Application are drawn in part to an affinity matrix comprising the KH-1 antigen, and thus can anticipate compounds containing the determinant of claim 108 and the compound of claim 110 (the Examiner had inadvertently typed "claim *108*", but Applicant believes the Examiner means in fact "claim *110*") wherein the set of indices (r, m, n) is (1, 0, 1) and R is an alkyl group.

Applicant notes that claims 5 and 10 in the '905 Application have been canceled in a Response under 37 C.F.R. § 1.111 filed February 27, 2003. However, the subject matter of canceled claims 5 and 10 has been re-introduced in new claims 64, 67, 69 and 74. Therefore, in an effort to expedite prosecution, the double patenting rejection will be addressed as if it were applied to new claims 64, 67, 69 and 74 in the '905 Application.

Applicant notes that new claims 64, 67, 69 and 74 in the '905 Application are drawn to an affinity matrix comprising tumor-associated carbohydrate- or glycopeptide-based antigens covalently bound to a solid support. The instant claims are not directed to carbohydrate compounds or compositions comprising carbohydrate compounds covalently bound to a solid support. Therefore, the instant claims are patentably distinct from claims 64, 67, 69 and 74 in the '905 Application. Accordingly, Applicant respectfully requests that the double patenting rejection be withdrawn.

Applicant thanks Examiner Canella for careful review and consideration of this case. If a telephone conversation would help clarify any issues, or help expedite prosecution of this case, Applicant invites the Examiner to contact the undersigned at (617) 248-5150.

Please charge any fees that may be required, or credit any overpayment, to our Deposit Account No. 03-1721.

Respectfully Submitted,

Dated: March 28, 2003

Nadège M. Lagneau, Ph.D.
Reg. No.: 51,908

Choate, Hall & Stewart
Exchange Place
53 State Street
Boston, MA 02109
(617) 248-5150

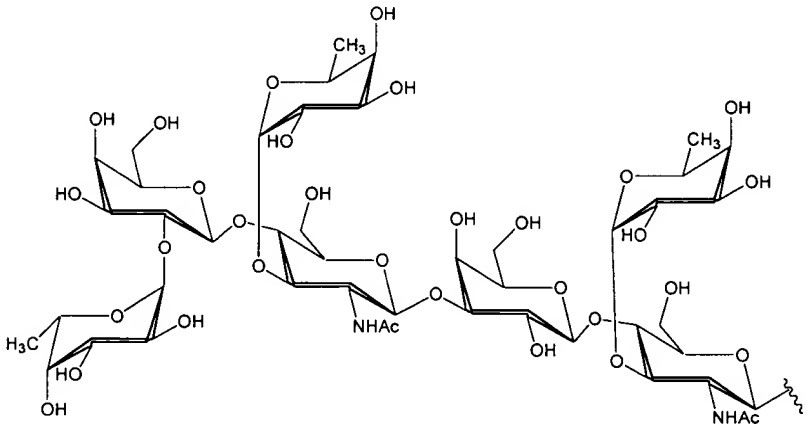
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231
on March 28, 2003
Kathy Hall Gagon

- APPENDIX A –

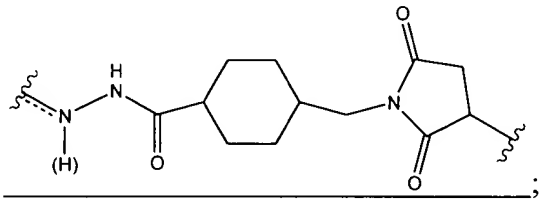
Version with Markings to Show Changes Made

A. Claim Replacements

108. A compound which contains a determinant having the structure:

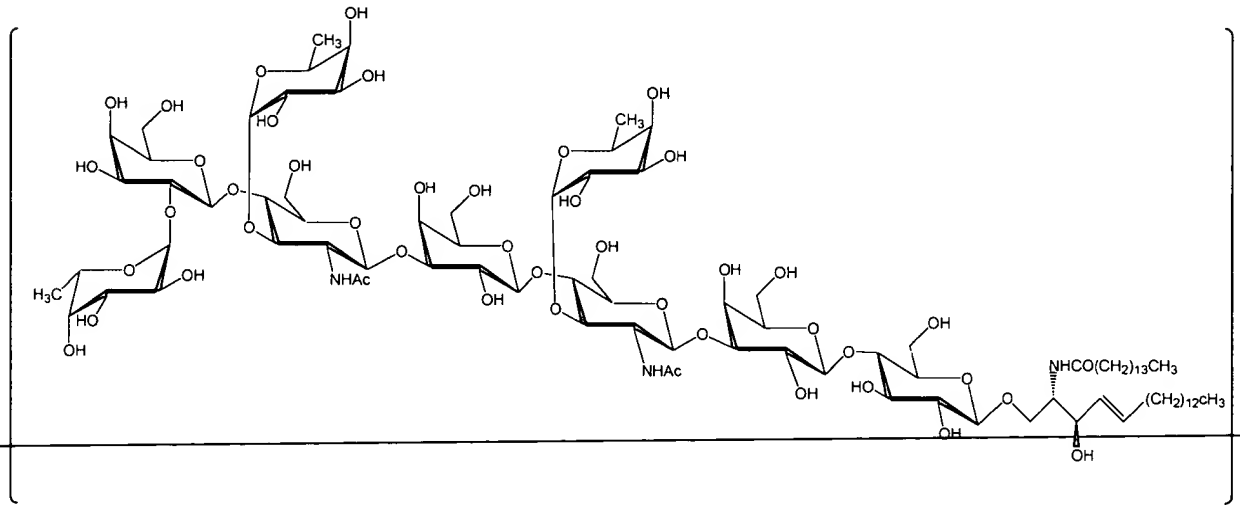


wherein the compound is bound to a suitable carrier protein or lipid, said compound being bound either directly or by a cross-linker selected from the group consisting of a succinimide and an M_2 linker having the structure:



;

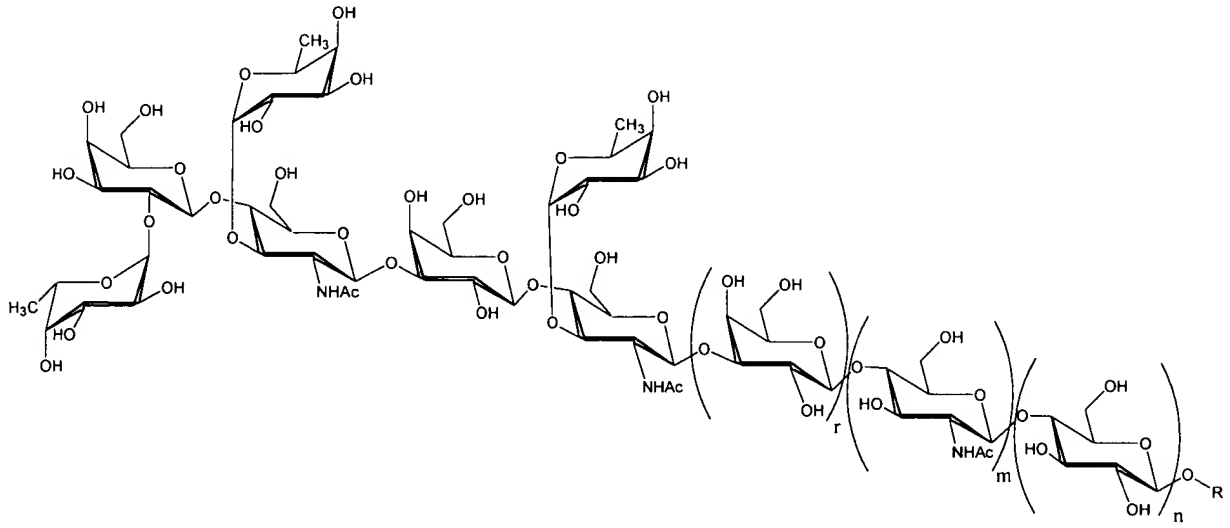
[with the proviso that the compound does not have the structure:]



with the proviso that when R is a ceramide moiety, the set of indices (r, m, n) is not

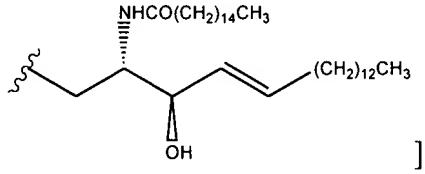
(1, 0, 1).

110. [The compound of claim 108 wherein the compound has] A compound having the structure:



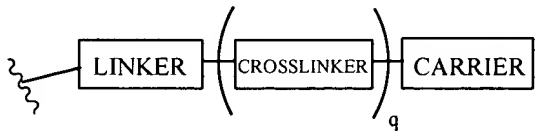
wherein r, m, and n are independently 0, 1, 2 or 3;

[wherein] R is H, substituted or unsubstituted [alkyl, aryl or] allyl, an amino acyl moiety, [a moiety having the structure:



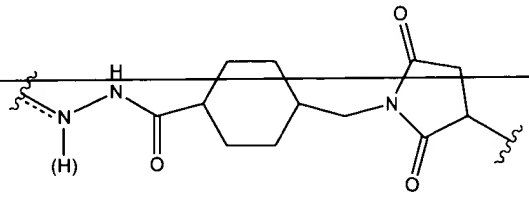
]

or a moiety having the structure:



wherein the linker is $-(CH_2)_s-CH_2-$ or $-(CH_2)_s-CH=$ where s is an integer between 0 and 8;

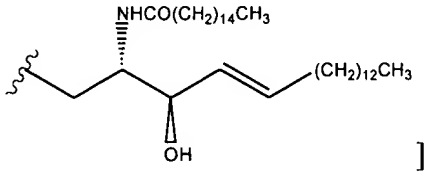
[wherein] the crosslinker is selected from the group consisting of a succinimide and an M_2 linker having the structure:



[wherein] q is 0 or 1; and

[and wherein] the carrier is a protein, peptide or lipid, and is optionally chemically modified prior to conjugation with the linker when q is 0, or with the crosslinker when q is 1;

with the proviso that when R is [the moiety having the structure:

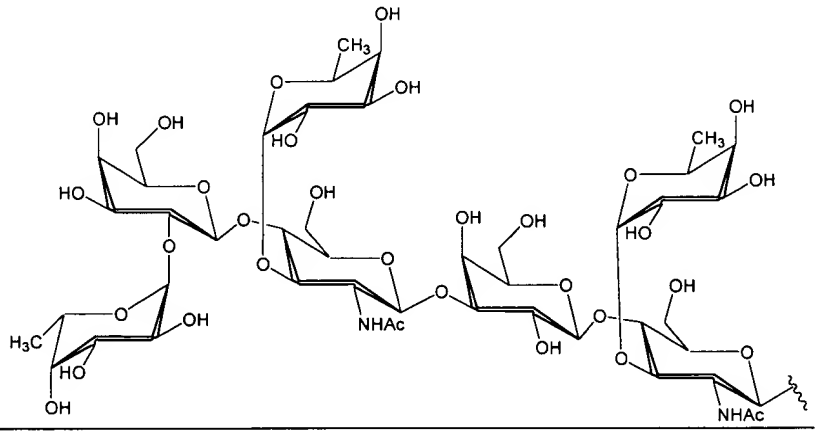


]

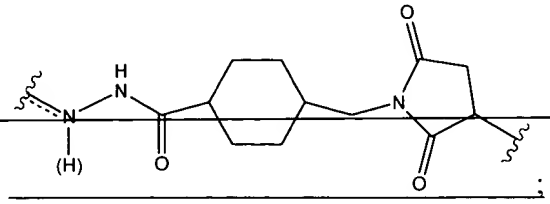
a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1).

111. The compound of claim [109] 108 or 110 wherein the protein is bovine serum albumin, polylysine, or keyhole limpet hemocyanin.

114. A composition comprising a compound [of claim 108; and optionally] which contains a determinant having the structure:



wherein the compound is bound to a suitable carrier protein or lipid, said compound being bound either directly or by a cross-linker selected from the group consisting of a succinimide and an M_2 linker having the structure:

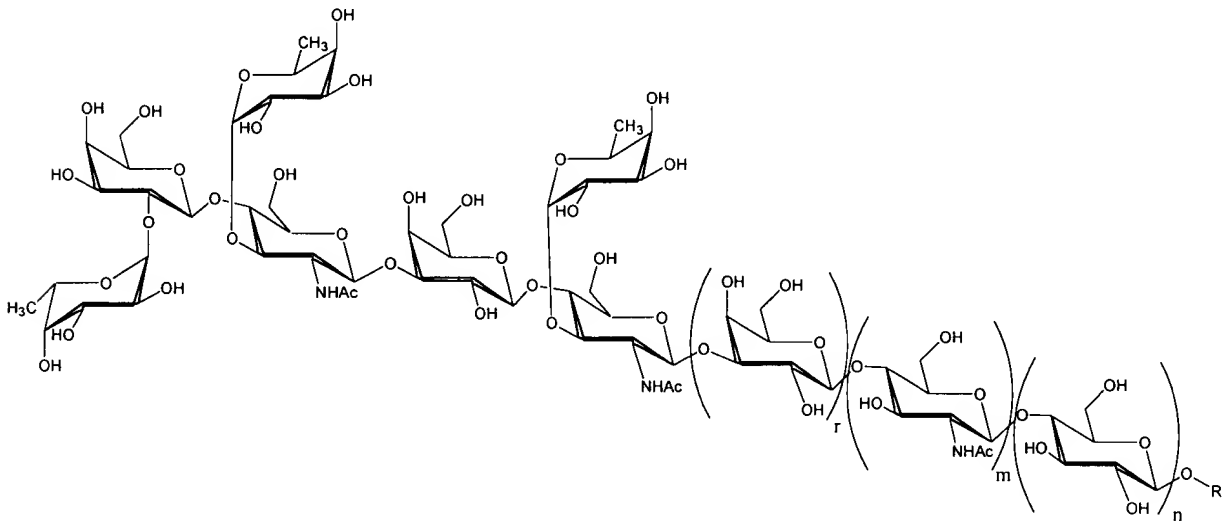


;

and an immunological adjuvant and/or a pharmaceutically acceptable carrier;

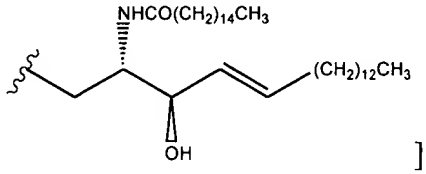
with the proviso that when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1).

116. [The composition of claim 114 wherein the compound has] A composition comprising a compound having the structure:



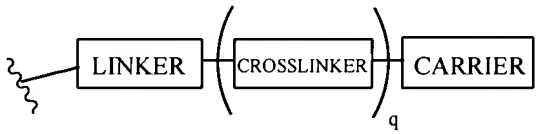
wherein r, m, and n are independently 0, 1, 2 or 3;

[wherein] R is H, substituted or unsubstituted alkyl, aryl or allyl, an amino acyl moiety, [a moiety having the structure:



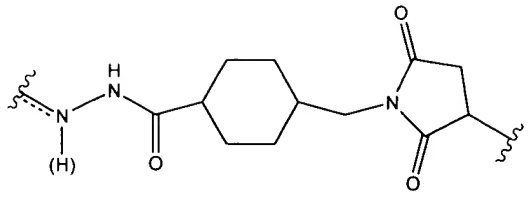
]

or a moiety having the structure:



wherein the linker is $-(CH_2)_s-CH_2-$ or $-(CH_2)_s-CH=$ where s is an integer between 0 and 8;

[wherein] the crosslinker is selected from the group consisting of a succinimide and an M_2 linker having the structure:

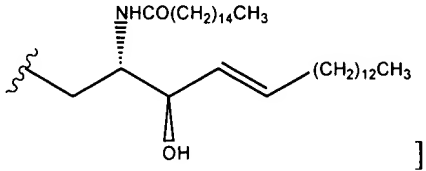


[wherein] q is 0 or 1; and

[and wherein] the carrier is a protein, peptide or lipid, and is optionally chemically modified prior to conjugation with the linker when q is 0, or with the crosslinker when q is 1;

and an immunological adjuvant and/or a pharmaceutically acceptable carrier;

with the proviso that when R is [the moiety having the structure:



]

a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1).

117. The composition of claim [115] 114 or 116 wherein the protein is bovine serum albumin, polylysine, or keyhole limpet hemocyanin.

118. The composition of claim 114 or 116 wherein the immunological adjuvant is bacteria or liposomes.

B. Paragraph Replacements

Paragraph on page 1, starting at line 6 and ending at line 12:

This application is [based on] a Divisional Application filed under 37 C.F.R. § 1.53(b) of Application Serial Number 09/042,280, filed January 13, 1998, which further claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application Serial No. 60/034,950, filed January 13, 1997[,]; the entire contents of [which] each of these applications are hereby incorporated by reference into this application. ~~This invention was made with government support under grants CA-28824-18,~~ GM-15240-02, GM-16291-01, HL-25848-14 and AI-16943 from the National Institutes of Health. Additionally, the present invention was supported in part by a fellowship from the United States

Army to Hyun Jin Kim (DAMD 17-97-1-7119). Accordingly, the U.S. Government has certain rights in the invention.

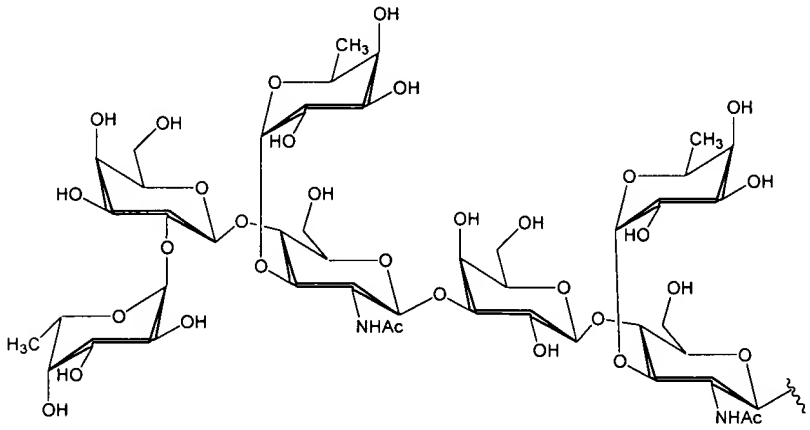
Paragraph on page 12, starting at line 21 and ending at line:

This antigen has been claimed to be a highly specific marker for malignancy and pre-malignancies involving colonic adenocarcinoma. The nonasaccharide character of **1** (Figure 1) is unique from a structural standpoint. The crystallographically derived presentation of the monoclonal antibody BR 96 bound to a Le^y tetrasaccharide glycoside has been reported. (Jeffery, P.D.; Bajorath, J.; Chang, C.Y.; Dale, Y.; Hellstrom, I.; Hellstrom, E.K.; Sheriff, S., *Nature Structural Biology*, **1995**, *2*, [456] 466.) The structure of the BR96:Le^y complex suggested that this antibody might also have the capacity to recognize higher order fucosylated arrays.

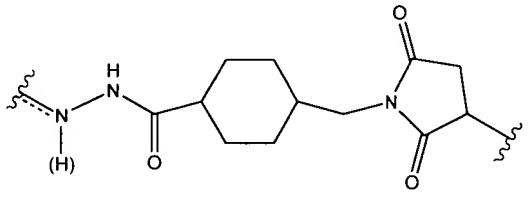
- APPENDIX B –

Claims as Pending After Entrance of the Present Amendment

108. A compound which contains a determinant having the structure:



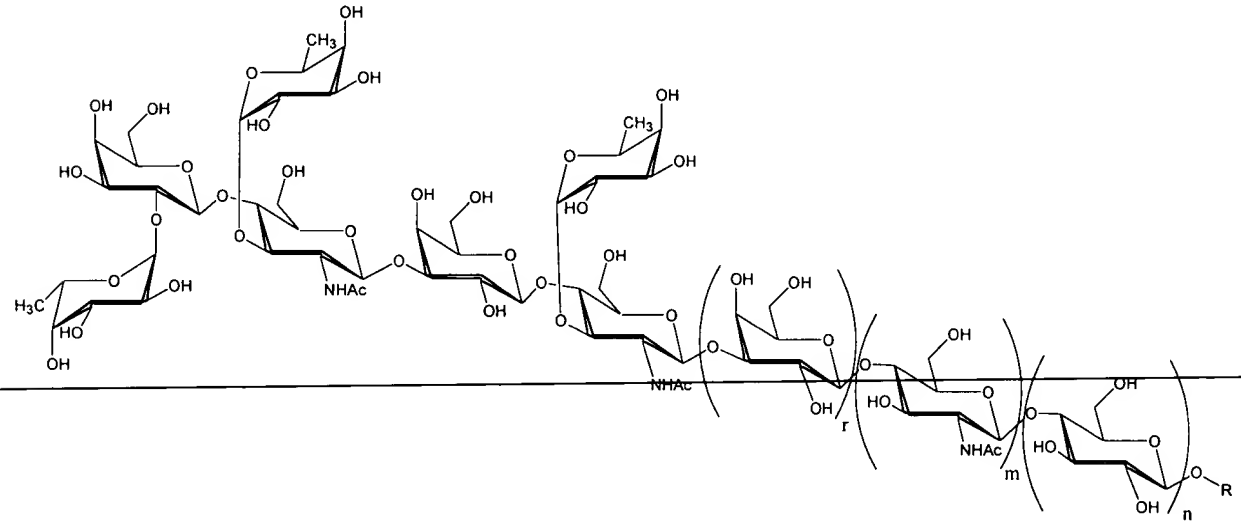
wherein the compound is bound to a suitable carrier protein or lipid, said compound being bound either directly or by a cross-linker selected from the group consisting of a succinimide and an M_2 linker having the structure:



;

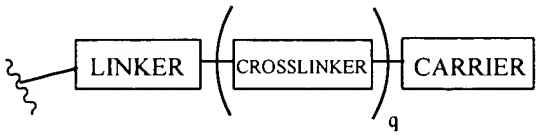
with the proviso that when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1).

110. A compound having the structure:



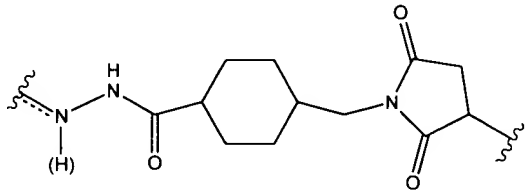
wherein r, m, and n are independently 0, 1, 2 or 3;

R is H, substituted or unsubstituted allyl, an amino acyl moiety, or a moiety having the structure:



wherein the linker is $-(CH_2)_s-CH_2-$ or $-(CH_2)_s-CH=$ where s is an integer between 0 and 8;

the crosslinker is selected from the group consisting of a succinimide and an M_2 linker having the structure:



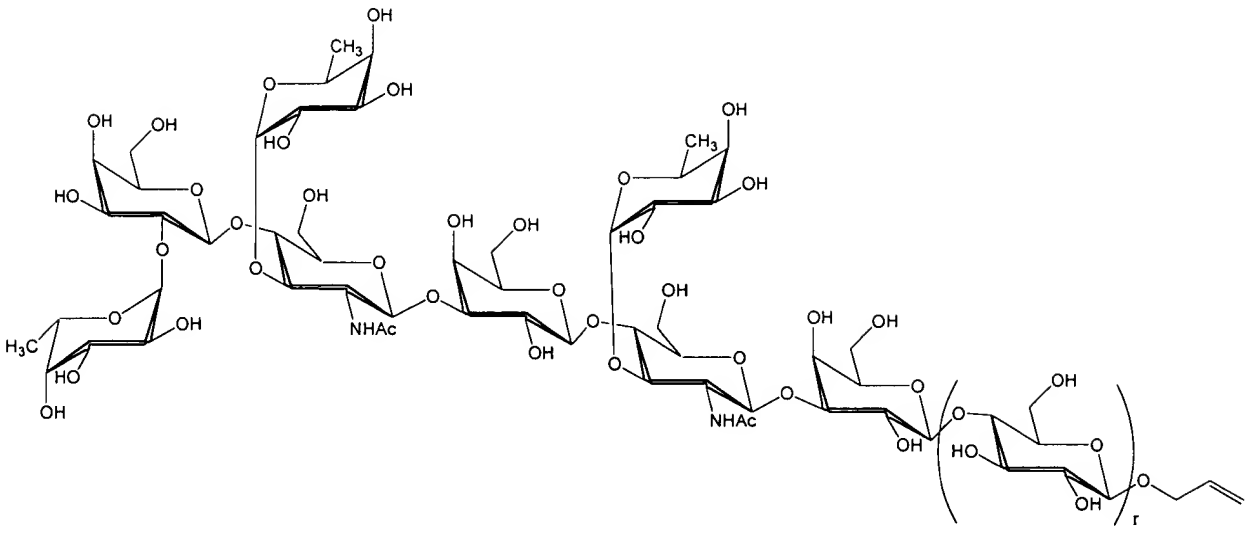
q is 0 or 1; and

the carrier is a protein, peptide or lipid, and is optionally chemically modified prior to conjugation with the linker when q is 0, or with the crosslinker when q is 1;

with the proviso that when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1).

111. The compound of claim 108 or 110 wherein the protein is bovine serum albumin, polylysine, or keyhole limpet hemocyanin.

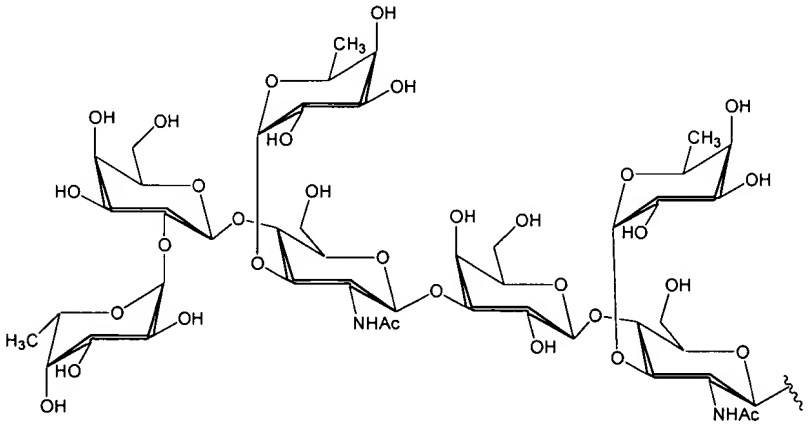
112. A compound having the structure:



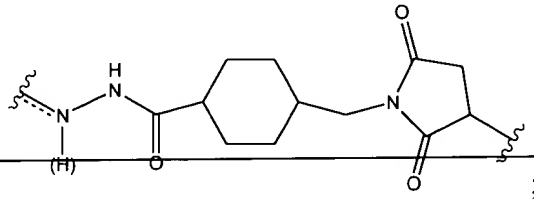
wherein r is 0, 1, 2, 3, or 4.

113. The compound of claim 112 wherein r is 1.

114. A composition comprising a compound which contains a determinant having the structure:



wherein the compound is bound to a suitable carrier protein or lipid, said compound being bound either directly or by a cross-linker selected from the group consisting of a succinimide and an M_2 linker having the structure:

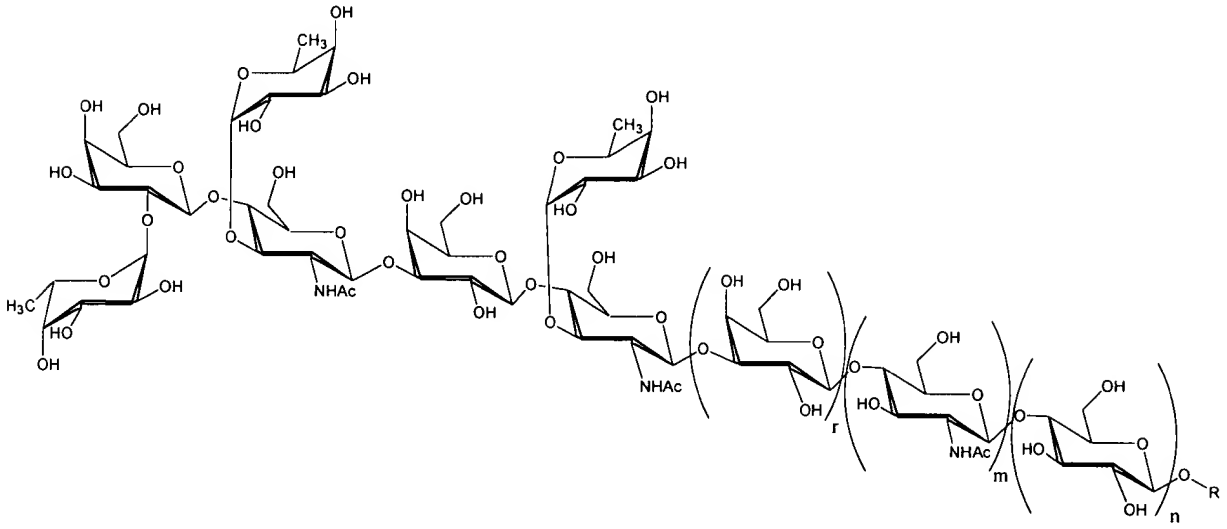


;

and an immunological adjuvant and/or a pharmaceutically acceptable carrier;

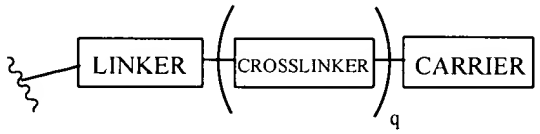
with the proviso that when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1).

116. A composition comprising a compound having the structure:



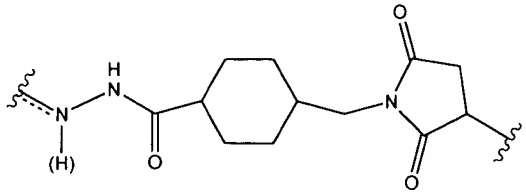
wherein r, m, and n are independently 0, 1, 2 or 3;

R is H, substituted or unsubstituted alkyl, aryl or allyl, an amino acyl moiety, or a moiety having the structure:



wherein the linker is $-(CH_2)_s-CH_2-$ or $-(CH_2)_s-CH=$ where s is an integer between 0 and 8;

the crosslinker is selected from the group consisting of a succinimide and an M_2 linker having the structure:



q is 0 or 1; and

the carrier is a protein, peptide or lipid, and is optionally chemically modified prior to conjugation with the linker when q is 0, or with the crosslinker when q is 1;

and an immunological adjuvant and/or a pharmaceutically acceptable carrier;

with the proviso that when R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0, 1).

117. The composition of claim 114 or 116 wherein the protein is bovine serum albumin, polylysine, or keyhole limpet hemocyanin.

118. The composition of claim 114 or 116 wherein the immunological adjuvant is bacteria or liposomes.

119. The composition of claim 118 wherein the adjuvant is *Salmonella minnesota* cells, bacille Calmette-Guerin or QS21.